

WHAT IS CLAIMED IS

1. A chronotherapy tablet comprising:
 - a substantially oblong core having a longitudinal axis, a first end and a second
 - 5 end, the core being comprised of at least two superposed layers of different
 - compositions wherein an interface between each layer is substantially perpendicular to
 - the longitudinal axis of the core and wherein at least one of the layers is a
 - pharmacologically active composition;
 - a coating which envelops the core, except for;
 - 10 at least one exposed release face of the core at at least one end of the core;
 - whereas upon oral administration the chronotherapy tablet effects the amelioration of
 - at least one chronobiological condition within 24 hours.
2. A chronotherapy tablet according to claim 1 comprising two layers of
- 15 pharmaceutical compositions separated by a layer of a different composition.
3. A chronotherapy tablet according to claim 1 comprising at least two layers of
- different pharmaceutical compositions.
- 20 4. A chronotherapy tablet according to claim 2 wherein two layers of different
- pharmaceutical compositions are separated by a layer of a different composition.
5. A chronotherapy tablet according to claim 3 wherein two layers of the same
- pharmaceutical compositions are separated by a layer of a different pharmaceutical
- 25 composition.
6. A chronotherapy tablet according to claim 4 comprising three layers of three
- different pharmaceutical compositions.

7. A chronotherapy tablet according to claim 2 comprising two layers of the same pharmaceutical composition separated by a layer of a different composition.
8. A chronotherapy tablet according to claim 1 wherein at least one of the layers of
5 compositions is a delay layer.
9. A chronotherapy tablet according to claim 3 wherein the first layer is a delay layer.
10. A chronotherapy tablet according to claim 4 wherein the layer of a different
10 composition is a delay layer.
11. A chronotherapy tablet according to claim 7 wherein the layer of a different composition is a delay layer.
12. A chronotherapy tablet according to claim 2 comprising at least three layers of
15 pharmaceutical compositions and two delay layers wherein the three layers of pharmaceutical compositions are each separated from each other by a delay layer.
13. A chronotherapy tablet according to claim 9 comprising
20 a second layer adjacent to the first layer which second layer comprises a therapeutically effective amount of a drug, and
a third layer adjacent to the second layer which third layer comprises a therapeutically effective amount of a drug, and
wherein the delay layer provides for substantially complete dissolution of the
25 delay layer between about 5 to about 9 hours after oral administration; and,
the drug is selected from the group consisting essentially of a nonsteroidal anti-inflammatory agent, an acetic acid derivative, acetylsalicylic acid, an indole derivative, sodium or potassium diclofenac, etodolac, indomethacin, ketorolac tromethamine, sulindac, tolmetin sodium, cyclooxygenase-2 inhibitor, celecoxib,

rofecoxib, a fenamate, mefenamic acid, floctafenine, an oxicam, meloxicam, piroxicam, piroxicam cyclodextrin, tenoxicam, a propionic acid derivative, fenoprofen, flurbiprofen, ibuprofen, ketoprofen, naproxen, naproxen sodium, oxaprozin, a tiaprofenic acid derivative, a salicylic acid derivative, and diflunisal.

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14. A chronotherapy tablet according to claim 13 wherein the second layer comprises a therapeutically effective amount of naproxen and the third layer comprises a therapeutically effective amount of naproxen.

10 15. A chronotherapy tablet according to claim 14 wherein the second layer comprises between about 175mg-675mg naproxen wherein said naproxen is substantially completely releasable within about 15 minutes of substantially complete dissolution of the delay layer under physiological conditions; and,

the third layer comprises between about 100mg-250mg naproxen that is
15 releasable, after substantially complete dissolution of the second layer, at a substantially constant rate over a period of about 5 hours under physiological conditions.

16. A chronotherapy tablet according to claim 15 wherein the second layer comprises
20 about 250mg naproxen and the third layer comprises about 125mg naproxen.

17. A chronotherapy tablet according to claim 12 wherein the first layer comprises a therapeutically effective amount of a drug, further comprising
a second layer adjacent to the first layer which second layer is a delay layer,
25 a third layer adjacent to the second layer which third layer comprises a therapeutically effective amount of a drug,
a fourth layer adjacent to the third layer which fourth layer is a delay layer,
a fifth layer adjacent to the fourth layer which fifth layer comprises a therapeutically effective amount of a drug,

wherein the second and fourth delay layers each provide for substantially complete dissolution of the delay layer to require between about 5 to about 9 hours, each, during dissolution of the core under physiological conditions; and,

the drug is selected from the group consisting essentially of an alpha-adrenergic
5 blocking agent, doxazosine mesylate, prazosin hydrochloride, terazosine hydrochloride dehydrate, an Alpha & Beta-adrenergic blocking agent, labetalol hydrochloride, a Beta-adrenergic blocking agent, a selective non ISA, atenolol, bisoprolol, esmolol hydrochloride, metoprolol hydrate, a Beta adrenergic blocking agent, a non selective ISA, oxprinolol hydrochloride, pindolol, a Beta-adrenergic
10 blocking agent, a non-selective non-ISA, nadolol, propranolol hydrochloride, timolol maleate, a centrally acting antiadrenergic agent, clonidine hydrochloride, methyl dopa, a Calcium Channel Blocker, amlodipine besylate, diltiazem hydrochloride, felodipine, nifedipine, verapamil Hydrochloride, a Vasolidator, diazoxide, epoprostenol sodium, hydralazine hydrochloride, minoxidil, a Potassium sparing
15 agent, amiloride hydrochloride, spironolactone, triamterene, an Angiotensin converting enzyme inhibitor, benazepril hydrochloride, captopril, enalapril maleate, lisinopril, ramipril, an Angiotensin II receptor antagonists, valsartan, candesartan cilexetil, and losartan potassium.

20 18. A chronotherapy tablet according to claim 13 wherein the first layer comprises a therapeutically effective amount of diltiazem, the third layer comprises a therapeutically effective amount of diltiazem, and the fifth layer comprises a therapeutically effective amount of diltiazem.

25 19. A chronotherapy tablet according to claim 18 wherein the first layer comprises between about 25mg-100mg diltiazem wherein said diltiazem within the first layer is substantially completely releasable within about 15 to about 25 minutes of oral administration, and

the third layer comprises between about 50mg-150mg diltiazem wherein said diltiazem within the third layer is substantially completely releasable within about 15 to about 25 minutes of substantially complete dissolution of the second layer; and,

the fifth layer comprises between about 80mg-200mg diltiazem wherein said
5 diltiazem within the fifth layer is substantially completely releasable within about 15 to about 25 minutes of substantially complete dissolution of the fourth layer.

20. A chronotherapy tablet according to claim 19 wherein the first layer comprises about 60mg diltiazem, the third layer comprises about 180mg diltiazem, and the fifth
10 layer comprises about 120mg diltiazem.

21. A chronotherapy tablet according to claim 2 wherein a first layer comprises a therapeutically effective amount of a drug,

a second layer adjacent to the first layer is a delay layer,
15 a third layer adjacent to the second layer comprises a therapeutically effective amount of a drug, and

wherein a therapeutically effective amount of a drug in the first layer is substantially completely releasable within about 15 minutes of oral administration of the tablet, and

20 the second layer provides for substantially complete dissolution of the layer to require between about 5 to about 9 hours during dissolution of the core under physiological conditions, and

a therapeutically effective amount of a drug in the third layer is substantially completely releasable within about 15 minutes of substantially complete dissolution of
25 the second layer; and,

wherein the drug is selected from the group consisting essentially of a beta-2-adrenergic agonist, salbutamol sulphate, terbutaline sulfate, a Systemic Xanthine, aminophyllin, and theophylline.

22. A chronotherapy tablet according to claim 21 wherein the first layer comprises a therapeutically effective amount of salbutamol, and the third layer comprises a therapeutically effective amount of salbutamol.
- 5 23. A chronotherapy tablet according to claim 22 wherein the first layer comprises between about 2mg to about 4mg salbutamol sulphate, and the third layer comprises between about 2mg to about 4mg salbutamol sulphate.
24. A method of treatment and/or prevention of a chronobiological condition
10 comprising orally administering a chronotherapy tablet comprising
a substantially oblong core having a longitudinal axis, a first end and a second end, the core being comprised of at least two superposed layers of different compositions wherein an interface between each layer is substantially perpendicular to the longitudinal axis of the core and wherein at least one of the layers is a
15 pharmacologically active composition;
a coating which envelops the core, except for;
at least one exposed release face of the core at at least one end of the core;
whereas upon oral administration the chronotherapy tablet effects the amelioration of at least one chronobiological condition within 24 hours.
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25. A method according to claim 24 of treatment and/or prevention of a chronobiological condition selected from the group consisting essentially of asthma, arthritis, gastrointestinal disorder, cardiovascular disease, and cancer.
- 25 26. A method according to claim 25 of treatment and/or prevention of a chronobiological condition of arthritis comprising orally administering a chronotherapy tablet comprising at least two layers of different pharmaceutical compositions and wherein the first layer is a delay layer, a second layer adjacent to the

first layer which second layer comprises a therapeutically effective amount of a drug,
and

a third layer adjacent to the second layer which third layer comprises a
therapeutically effective amount of a drug, and

5 wherein the delay layer provides for substantially complete dissolution of the
delay layer between about 5 to about 9 hours after oral administration; and,

the drug is selected from the group consisting essentially of a nonsteroidal anti-
inflammatory agent, an acetic acid derivative, acetylsalicylic acid, an indole
derivative, sodium or potassium diclofenac, etodolac, indomethacin, ketorolac
10 tromethamine, sulindac, tolmetin sodium, cyclooxygenase-2 inhibitor, celecoxib,
rofecoxib, a fenamate, mefenamic acid, floctafenine, an oxicam, meloxicam,
piroxicam, piroxicam cyclodextrin, tenoxicam, a propionic acid derivative,
fenoprofen, flurbiprofen, ibuprofen, ketoprofen, naproxen, naproxen sodium,
oxaprozin, a tiaprofenic acid derivative, a salicylic acid derivative, and diflunisal.

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27. A method according to claim 25 of treatment and/or prevention of a
chronobiological condition of cardiovascular disease comprising orally administering
a chronotherapy tablet comprising a first layer which comprises a therapeutically
effective amount of a drug,

20 a second layer adjacent to the first layer which second layer is a delay layer,

a third layer adjacent to the second layer which third layer comprises a
therapeutically effective amount of a drug,

a fourth layer adjacent to the third layer which fourth layer is a delay layer,

a fifth layer adjacent to the fourth layer which fifth layer comprises a

25 therapeutically effective amount of a drug,

wherein the second and fourth delay layers each provide for substantially
complete dissolution of the delay layer to require between about 5 to about 9 hours,
each, during dissolution of the core under physiological conditions; and,

the drug is selected from the group consisting essentially of an alpha-adrenergic blocking agent, doxazosine mesylate, prazosin hydrochloride, terazosine hydrochloride dehydrate, an Alpha & Beta-adrenergic blocking agent, labetalol hydrochloride, a Beta-adrenergic blocking agent, a selective non ISA, atenolol, 5 bisoprolol, esmolol hydrochloride, metoprolol hydrate, a Beta adrenergic blocking agent, a non selective ISA, oxprinolol hydrochloride, pindolol, a Beta-adrenergic blocking agent, a non-selective non-ISA, nadolol, propanolol hydrochloride, timolol maleate, a centrally acting antiadrenergic agent, clonidine hydrochloride, methyldopa, a Calcium Channel Blocker, amlodipine besylate, diltiazem hydrochloride, 10 felodipine, nifedipine, verapamil Hydrochloride, a Vasolidator, diazoxide, epoprostenol sodium, hydralazine hydrochloride, minoxidil, nitroglycerine, a Potassium sparing agent, amiloride hydrochloride, spironolactone, triamterene, an Angiotensin converting enzyme inhibitor, benazipril hydrochloride, captopril, enalapril maleate, lisinopril, ramipril, an Angiotensin II receptor antagonists, 15 valsartan, candesartan cilexetil, and losartan potassium.

28. A method according to claim 25 of treatment and/or prevention of a chronobiological condition of asthma comprising orally administering a chronotherapy tablet comprising a first layer which comprises a therapeutically effective amount of a 20 drug,

a second layer adjacent to the first layer which is a delay layer,

a third layer adjacent to the second layer which comprises a therapeutically effective amount of a drug, and

wherein a therapeutically effective amount of a drug in the first layer is 25 substantially completely releasable within about 15 minutes of oral administration of the tablet, and

the second layer provides for substantially complete dissolution of the layer to require between about 5 to about 9 hours during dissolution of the core under physiological conditions, and

a therapeutically effective amount of a drug in the third layer is substantially completely releasable within about 15 minutes of substantially complete dissolution of the second layer; and,

wherein the drug is selected from the group consisting essentially of a beta-2-
5 adrenergic agonist, salbutamol sulphate, terbutaline sulfate, a Systemic Xanthine, aminophyllin, and theophylline.

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